

IN VITRO STUDY ON THE ADSORPTION OF RIFAMPICIN
FROM AQUEOUS SOLUTION

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ABSTRACT

The adsorption of rifampicin has been investigated onto kaolin, talc, magnesium trisilicate, magnesium oxide and avicel pH 101. Adsorption of rifampicin was markedly dependent on the nature of the adsorbent used. The amount of rifampicin adsorbed was found to be in obedience with both Langmuir and Freundlich equations. The extent of the amount adsorbed was correlated with the adsorbent structure. The decreasing order for the affinity of rifampicin to the selected adsorbents was as follows: kaolin > talc > magnesium trisilicate > avicel pH 101 > magnesium oxide.

The effect of different concentrations of polysorbate 80 on the amount of rifampicin adsorbed onto activated charcoal surface has revealed that as the surfactant concentration was increased the amount of the drug adsorbed was correspondingly decreased. The mechanism through which the decrease in the extent of adsorption, in the presence of the surfactant, has been discussed.

INTRODUCTION

Adsorption study of medicinal substances from their aqueous solutions is valuable from the pharmaceutical point of view. The adsorption studies are usually carried out for the following three reasons : a) to investigate the probability of a drug molecules to be adsorbed onto the inner wall of the container during the storage period¹, b) to look for an adsorbent suitable for sustained release preparations² and c) to find out a correlation between the adsorption of a drug molecules and both the rate and extent of its absorption from GI tract^{3,4}.

A knowledge of the in_vitro adsorption characteristics of a drug might be valuable so as to predict its in_vivo effect. The ability of certain adsorbents to interfere with a drug absorption is known through their use as antidotes for certain types of toxicity⁵.

Since the gut membrane is considered to be hydrophobic in nature, the absorption process of a drug molecules is considered to proceed through adsorption of the drug molecules onto the GI tract surface followed by transport through the membrane⁶. Recently, it is common for the physicians to prescribe two or more drugs for the same patient. The undesired effect due to concomitant administration of more than one drug arises from the fact that, the surface of coadministered water-insoluble drug like magnesium oxide, may adsorb a part of the drug molecules inside the GI tract resulting in a formation of a bound drug which is not ready to be absorbed⁷. The adsorption of some medicinally active compounds by various types of adsorbents has been reported^{3,6,8-17}.

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The purpose of the present work was to investigate the extent and variation in the adsorption of rifampicin on some selected adsorbents. Also, the study comprised the effect of different concentrations of polysorbate 80 on the adsorption capacity of charcoal towards rifampicin molecules.

EXPERIMENTAL

Materials

Rifampicin (Lepetit, Italy), magnesium oxide (Carlo Erba, Italy) magnesium trisilicate (El-Nasr Pharm. Co., Egypt), activated charcoal (Merck), avicel pH 101 (FMC Corp., USA), kaolin and talc (B.P. grade) polysorbate 80 (Merck), citric acid (Merck) disodium hydrogen phosphate (El-Nasr Pharm. Co., Egypt) and dimethylformamide (BDH).

Methods

(A) Determination of rifampicin adsorption isotherms.

All the experimental studies were carried out at pH 6. The selection of that pH value was, actually, based on some consideration regarding the stability of rifampicin in aqueous solution¹⁸. The adsorbents tested were avicel pH 101, magnesium oxide, magnesium trisilicate, kaolin, talc and activated charcoal. The adsorption isotherms were carried out in the following manner:

An accurately weighed 0.5 g of each adsorbent was placed into a series of five glass stoppered rotating tubes. A stock rifampicin solution (1 mg/ml) was prepared by dissolving 25 mg rifampicin in 2 ml dimethylformamide and the volume was completed to 25 ml with McIlvaine's buffer previously prepared at pH 6. Different initial concentrations of rifampicin solution (0.4, 0.8, 1.2, 1.6 and 2 mg/20 ml)

were prepared by appropriate dilution of suitable samples with McIlvaines buffer at the same pH value. A 20 ml sample of each solution was transferred into a rotating tube containing the adsorbent. The tubes were placed in a thermostatically controlled water bath operating at 30°C and allowed to be rotated at 50 rpm for 4 hours (the time required for equilibration). At the end of the experiment suitable portions of the suspensions were centrifuged and the clear supernate was assayed colorimetrically at 475 nm, after appropriate dilution with distilled water, for its rifampicin content. The absorbance was measured by Shimadzu double beam spectrophotometer (Japan). Each experiment was carried out in duplicate and the average amount of the drug adsorbed was calculated by the difference between the initial and equilibrium concentrations.

(B) Adsorption isotherms of rifampicin onto charcoal in the presence of different concentrations of polysorbate 80.

The experiments were carried out similarly to that previously described under (A). The sole difference is that the amount of charcoal used was 0.1 g/20 ml and the initial concentrations of rifampicin were 20, 22, 24, 26 and 28 mg/20 ml. The vehicle used was McIlvaines buffer at pH 6 containing 0.0001, 0.0005 and 0.005% w/v polysorbate 80. A blank for each experiment was treated similarly.

RESULTS AND DISCUSSION

The amount of rifampicin adsorbed per unit weight of adsorbent was calculated as :

$$M = \frac{X}{m} = \frac{V \cdot \Delta C}{m} \quad \text{eq. 1}$$

where V is the volume of rifampicin aqueous solution (20 ml), ΔC is the difference between the initial and the equilibrium

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concentrations while m is the weight of adsorbent, in gram, used.

Throughout this study it was assumed that the amount of the aqueous medium adsorbed by each adsorbent is negligible, otherwise the uptake of water molecules by an adsorbent would change the equilibrium concentration of the drug. For this reason the adsorption investigated is actually the apparent one.

The adsorption of rifampicin to different adsorbents was found to be in agreement with the Langmuir equation¹⁹.

$$M = \frac{a b C_e}{1 + b C_e} \quad \text{eq. 2}$$

where M is as defined in eq. 1, a is the amount of adsorbate adsorbed when the entire surface of the adsorbent is covered by a monolayer, b is the equilibrium constant for the adsorption process and C_e is the equilibrium concentration.

Equation 2 may be rearranged as:

$$\frac{C_e}{M} = \frac{1}{a} C_e + \frac{1}{ab} \quad \text{eq. 3}$$

or

$$\frac{1}{M} = \frac{1}{ab} \frac{1}{C_e} + \frac{1}{a} \quad \text{eq. 4}$$

According to equation 3 when $\frac{C_e}{M}$ is plotted versus C_e , a straight line will be obtained with a slope of $\frac{1}{a}$ and an intercept of $\frac{1}{ab}$. The reciprocal of the slope a , which is usually termed the limiting adsorptive capacity in mg/g, is usually used as a parameter to compare between the adsorptive capacities of the selected adsorbents towards rifampicin molecules.

The results of the adsorption measurements according to eq. 3 are presented graphically in figure 1. This figure shows that adsorption of rifampicin onto the investigated adsorbents was in obedience with the Langmuir adsorption equation 3. It could be observed from this figure that the degree and extent of adsorption of rifampicin is markedly dependent on the type of sorbent used. The superior adsorbent was found to be kaolin.

The results were also plotted according to equation 4 and graphically presented in figure 2. The figure indicates, also, that the plotting of the data obeyed the Langmuir equation 4. The limiting adsorptive capacities (a values) of the adsorbents were calculated and the average values obtained from both figures 1 and 2 were illustrated in Table 1.

Also, the results were plotted according to Freundlich equation which is given in a linear form as:

$$\log \frac{X}{m} = \log K + N \log C_e \quad \text{eq. 5}$$

where C_e , X and m were defined previously, K is a constant which gives a rough measure of the relative adsorbent capacity for a given drug, while N gives a general idea for the affinity of the adsorbate for adsorbent, Figure 3 shows that the adsorption of rifampicin by the various adsorbents obeyed the Freundlich equation. The calculated values of the slope (N) and the intercept ($\log K$) are surveyed in Table 1. The value of the intercept was taken as a parameter to compare between the different adsorbents. From figures 1-3 and Table 1, it could be observed that rifampicin is much highly adsorbed onto the kaolin surface than onto the other tested adsorbents.

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The adsorbents could be ranked in a decreasing order according to their adsorptive capacities, a , as follows: kaolin > talc > magnesium trisilicate > avicel pH 101 > magnesium oxide. The same order of arrangement was also obtained when the adsorbents were arranged according to their intercept values ($\log K$) in the Freundlich plot.

The structure of kaolin, $Al_4Si_4O_{10}(OH)_8$, is composed of two basic units. One is an octahedron of oxygen atoms (hydroxyl groups) surrounding the central aluminium atom. The second unit composed of four oxygen atoms situated at the corners of a regular tetrahedron, with the silicon atom in the center. The higher degree of adsorption exhibited by kaolin may be explained on the basis that rifampicin molecule having two phenolic groups in para position. These groups create a negative center on the aromatic ring. It was reported that rifampicin interacts with aluminium chloride and forms a cherry-red product²⁰. Therefore, the high adsorptive power of kaolin may be due to the electrostatic attraction between aluminium ion, in kaolin molecule, and the negative center in rifampicin aromatic ring.

The data revealed that rifampicin molecules were identically adsorbed onto both talc and magnesium trisilicate. This behaviour could be explained on the consideration that both the hydrous magnesium silicate and magnesium trisilicate possess the same ions. The surface structure of silica adsorbents is characterized by the presence of silanol groups which are capable for the formation of hydrogen bonds with rifampicin molecules.

There is a plenty of literatures stating that the microcrystallin cellulose, Avicel, having a negative charge

on its surface²¹⁻²³. This is most likely due to ionization of carboxylate groups on its surface. The pka of these carboxylic groups is 4^{21} . Since the adsorption study in this work was carried out at pH 6, the number of the negatively charged carboxylate groups on the surface of avicel pH 101 increased. Therefore, the adsorption mechanism between avicel pH 101 and rifampicin may be presumably due to hydrogen bond formation between the negative surface of avicel and the created positive charges on the hydrogen of the phenolic groups.

The adsorption of rifampicin onto magnesium oxide surface may be probably due to hydrogen bond formation between the electron-accepting hydrogen atoms of the hydroxyl groups in rifampicin molecules and the negative oxygen atoms situated on the surface of magnesium oxide. The pH value of the final supernate of magnesium oxide suspension was approximately 10.8. The decrease in the extent of adsorption of rifampicin molecules on the surface of magnesium oxide is most likely due to the increase in the pH value of the supernate. Since the basic pK_a of rifampicin is about 7.9, so, at pH 6 99.84% of the drug exists in an ionized form. Accordingly the attraction force between rifampicin molecules and the negative surface of magnesium oxide is completely reduced. This explains why magnesium oxide exhibited the least adsorptive capacity towards rifampicin.

Adsorption of rifampicin onto activated charcoal in the presence of different concentrations of ploysorbate 80.

The results of rifampicin adsorption onto charcoal are graphically presented in figures 4-6. It could be observed from figures 4 and 5 that the adsorption of rifam-

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picin by charcoal followed the Langmuir equations 3 and 4. The results were plotted according to Freundlich equation, and it was found that the results were in agreement with the Freundlich plot. Both the Langmuir and Freundlich constants are tabulated in Table 2. The data revealed that as the concentration of polysorbate 80 increased the amount of rifampicin adsorbed was correspondingly decreased.

To elucidate the reason of the adsorption reduction by polysorbate 80 it could be postulated that the surfactant molecules may compete with the drug for the vacant sites on the surface of charcoal. This is confirmed by the observation that as the surfactant concentration increased the amount of the drug adsorbed was consequently decreased. This was due to the increase in the amount of surfactant molecules adsorbed on the surface of charcoal. It was reported that the adsorption capacity of charcoal is due mainly to its very large hydrophobic surface area on which the drug in its unionized form will be best adsorbed²⁴. The decrease in the amount of rifampicin adsorbed by charcoal in the presence of polysorbate 80 may be due to an increase in rifampicin solubility in polysorbate solution than in water. Therefore, as the surfactant concentration was increased the affinity of rifampicin molecules to the aqueous phase was increased.

Table 1. Langmuir and Freundlich Constants for the Adsorption of Rifamicin by Different Adsorbents at pH6 and 30°C.

Adsorbent	Langmuir constants		Freundlich constants	
	a (mg/g)	b (20 ml/mg)	slope (N)	intercept (log K)
Kaolin	2.53	3.60	0.355	0.299
Talc	1.29	8.75	0.271	0.056
Magnesium trisilicate	1.27	1.15	0.576	-0.180
Avicel pH 101	1.11	0.29	0.807	-0.608
Magnesium oxide	0.48	0.63	0.658	-0.743

Table 2. Langmuir and Freundlich Constants for the Adsorption of Rifampicin by Activated Charcoal in Presence of Different Concentrations of Polysorbate 80 at pH 6 and 30°C.

Polysorbate 80 concentration (% w/v)	Langmuir constants		Freundlich constants	
	a (mg/g)	b (20 ml/mg)	slope (N)	intercept (log K)
0	200	0.75	0.171	2.10
0.0001	174	0.90	0.106	2.06
0.0005	143	1.01	0.184	1.90
0.005	137	0.26	0.234	1.77

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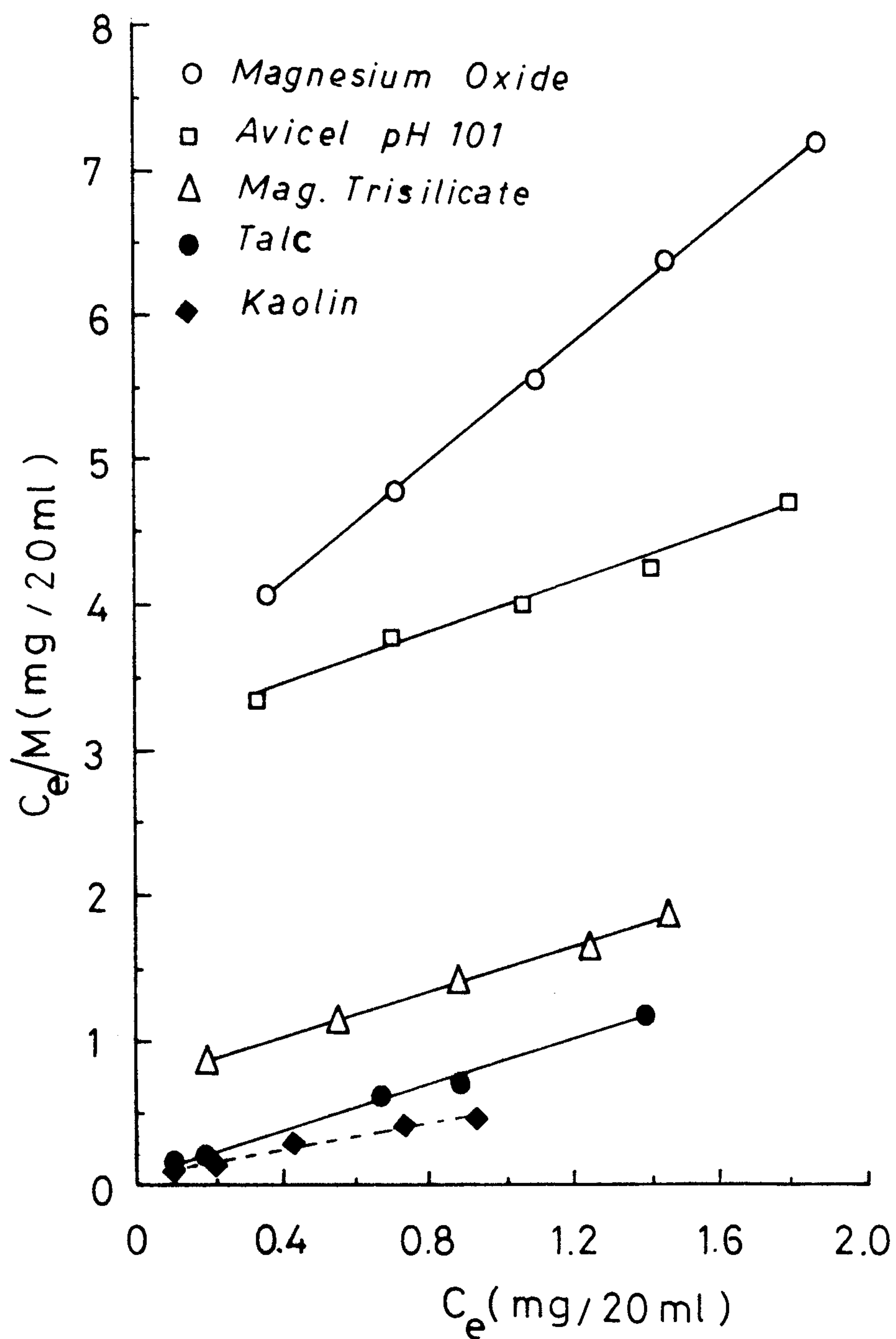


Fig. 1 : Langmuir Adsorption Isotherm for Rifampicin on Various Adsorbents.

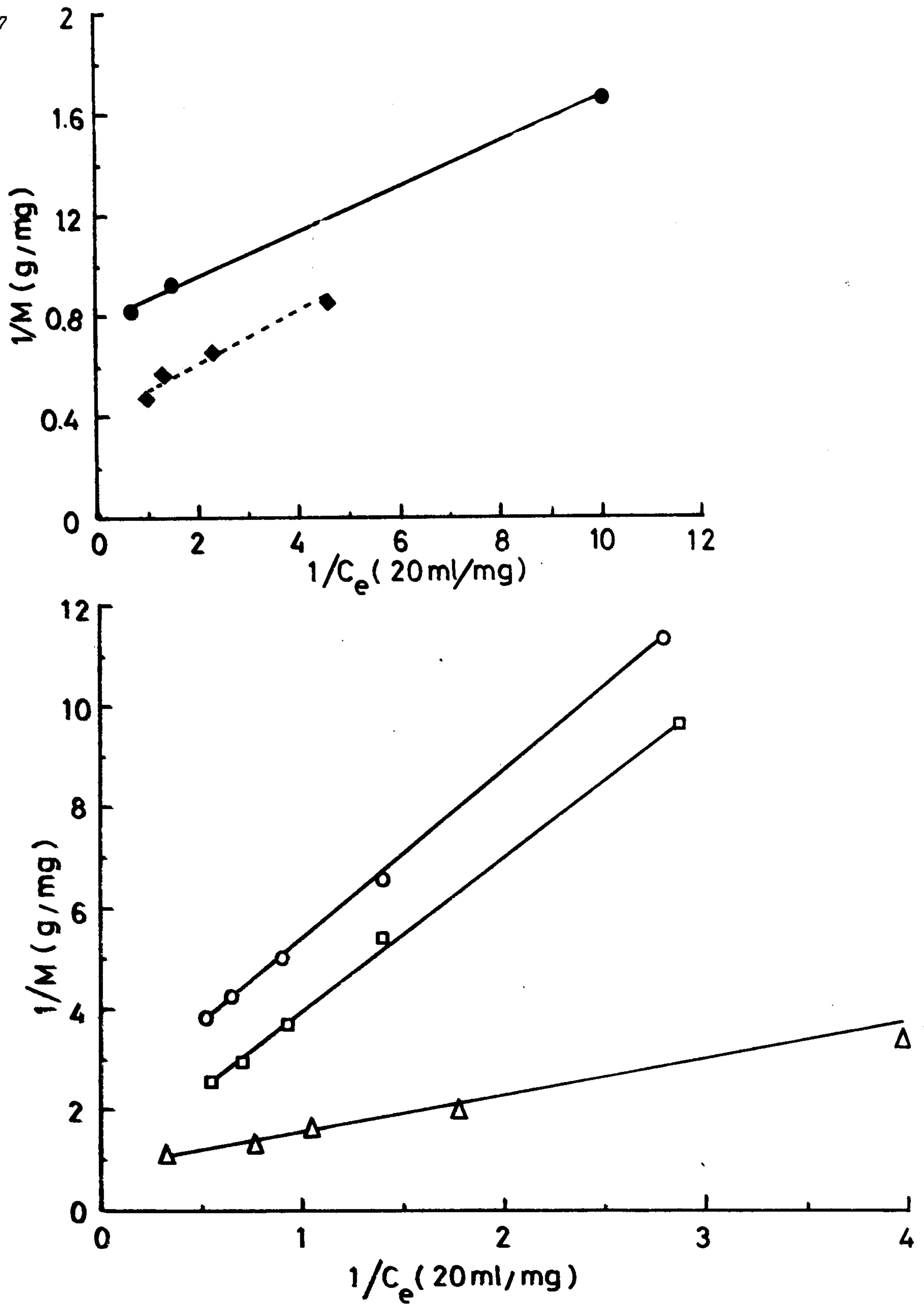


Fig. 2 : Langmuir Adsorption Isotherm for Rifampicin on Various Adsorbents.

Key : The same as Fig. 1.

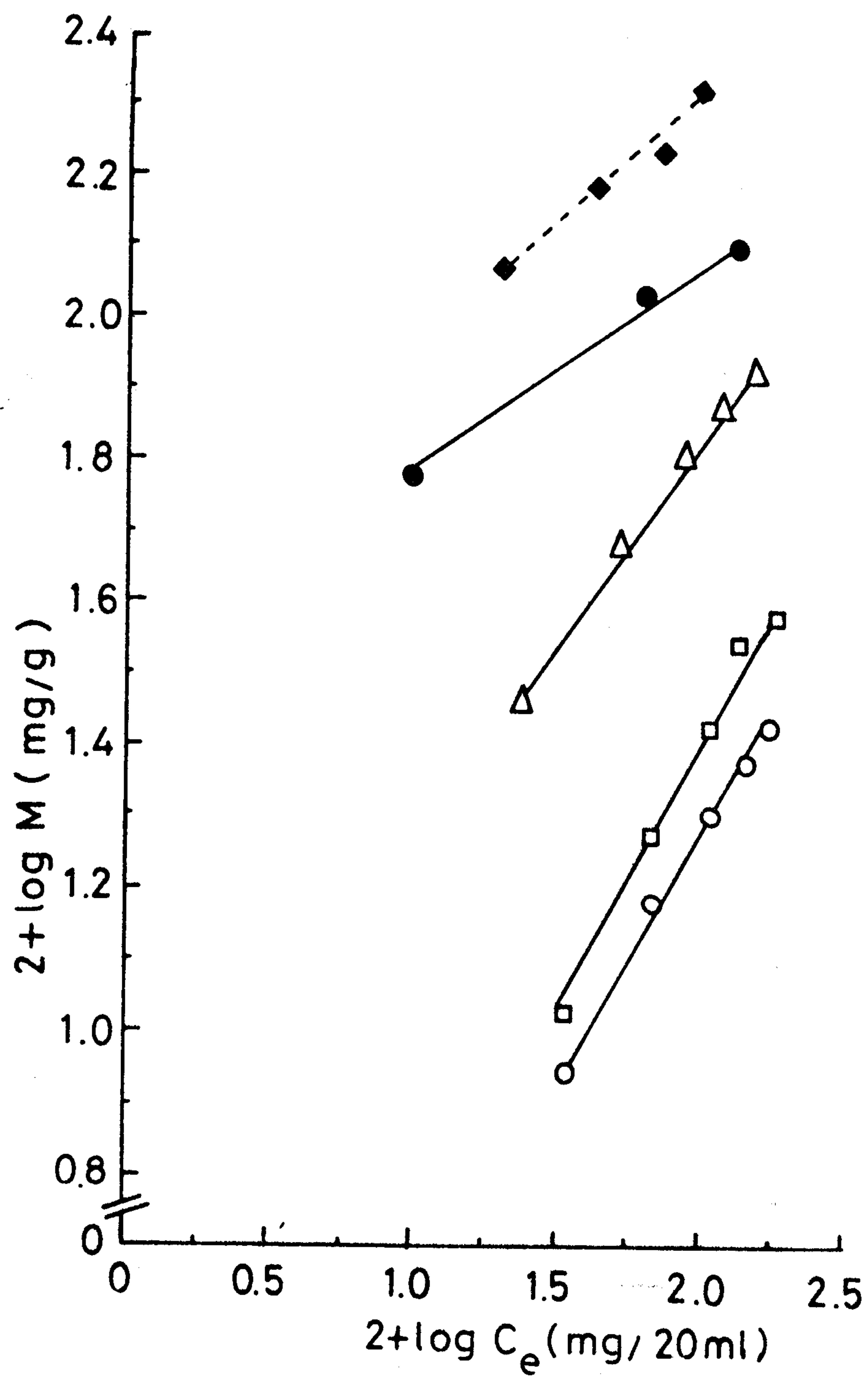


Fig. 3 : Freundlich Adsorption Isotherm for Rifampicin on Various Adsorbents.

Key : The same as Fig. 1.

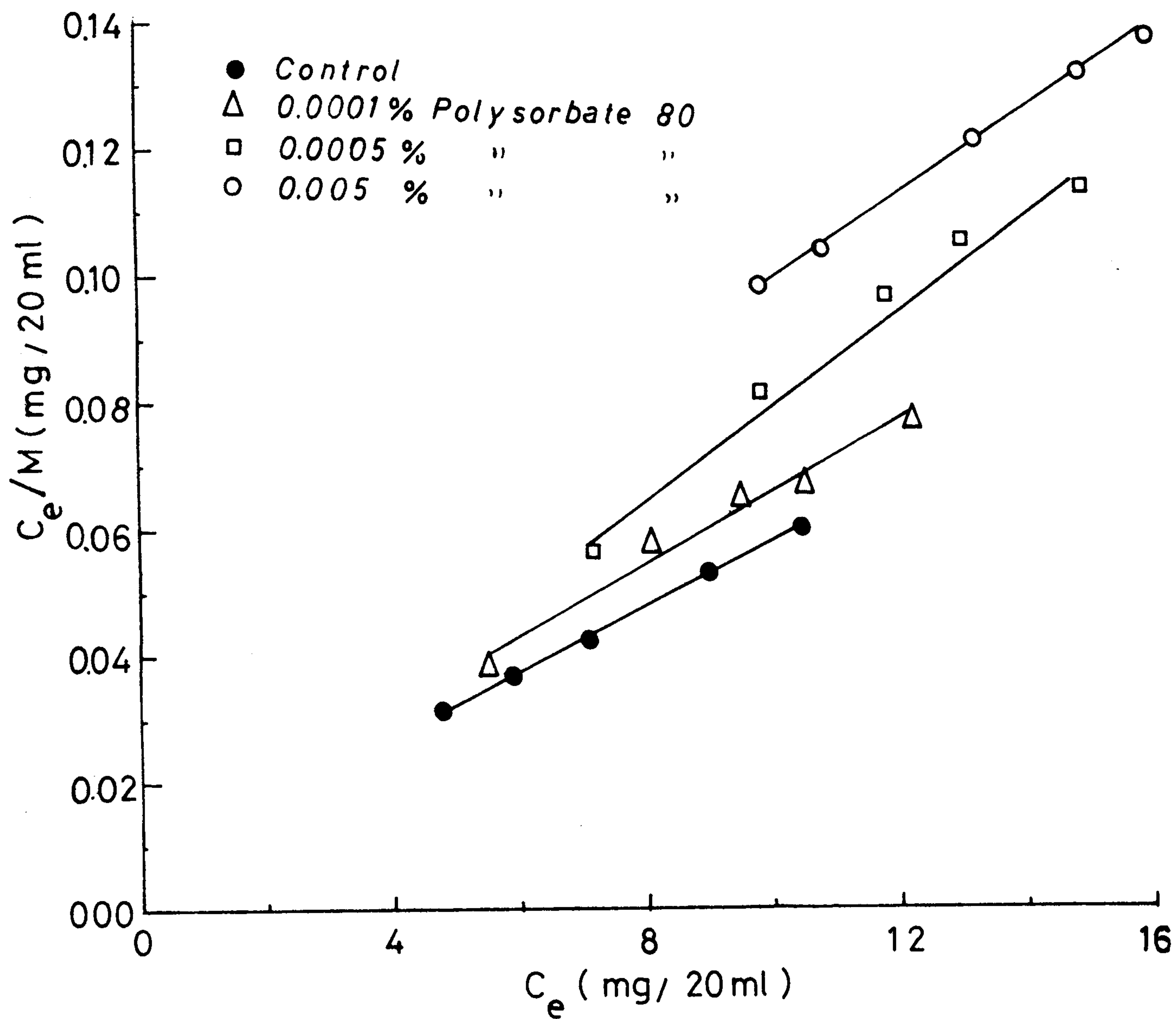


Fig. 4 : Langmuir Adsorption Isotherm for Rifampicin on Activated Charcoal and in the Presence of Different Concentrations of Polysorbate 80.

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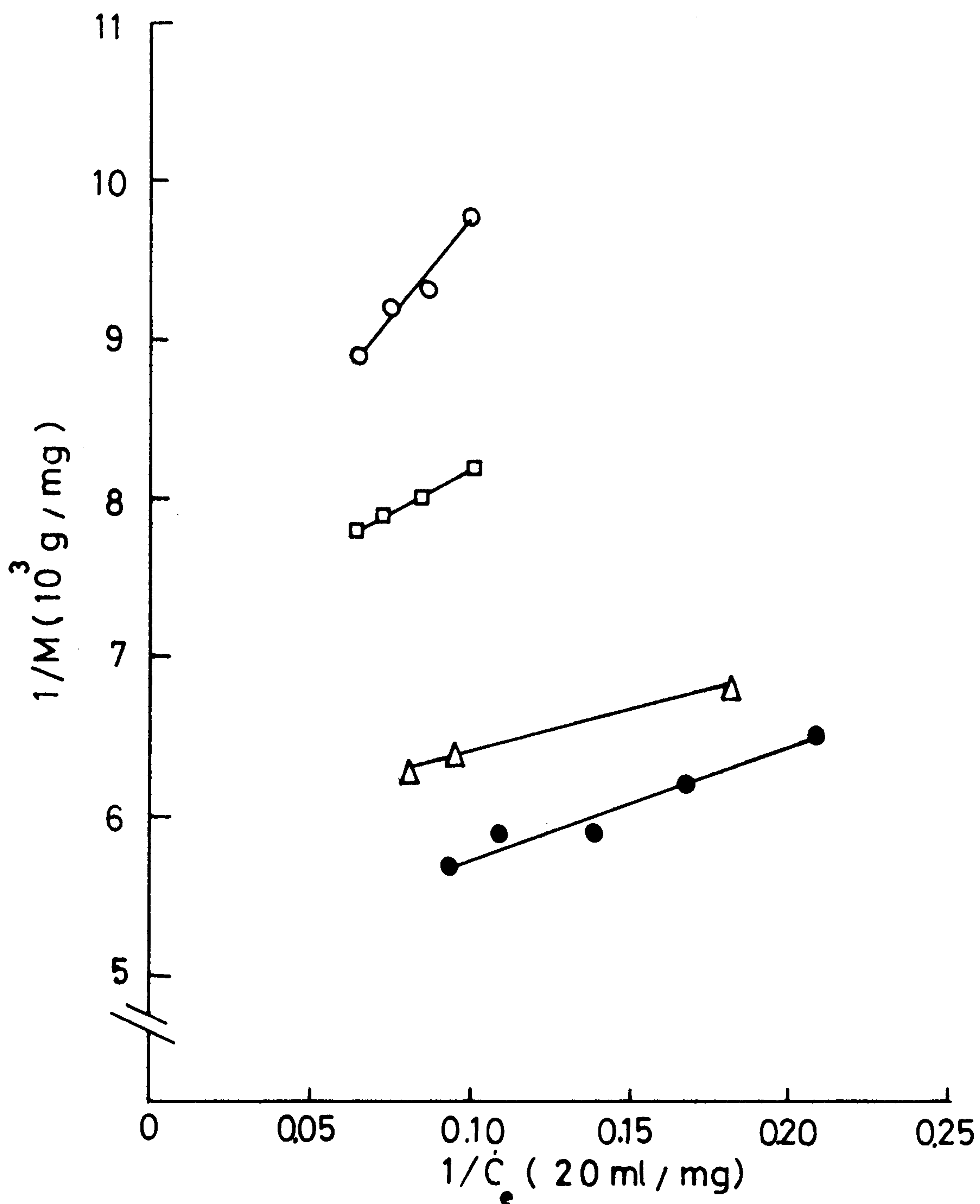


Fig. 5 : Langmuir Adsorption Isotherm for Rifampicin on Activated Charcoal and in the Presence of Different Concentrations of Polysorbate 80.

Key : The same as Fig. 4.

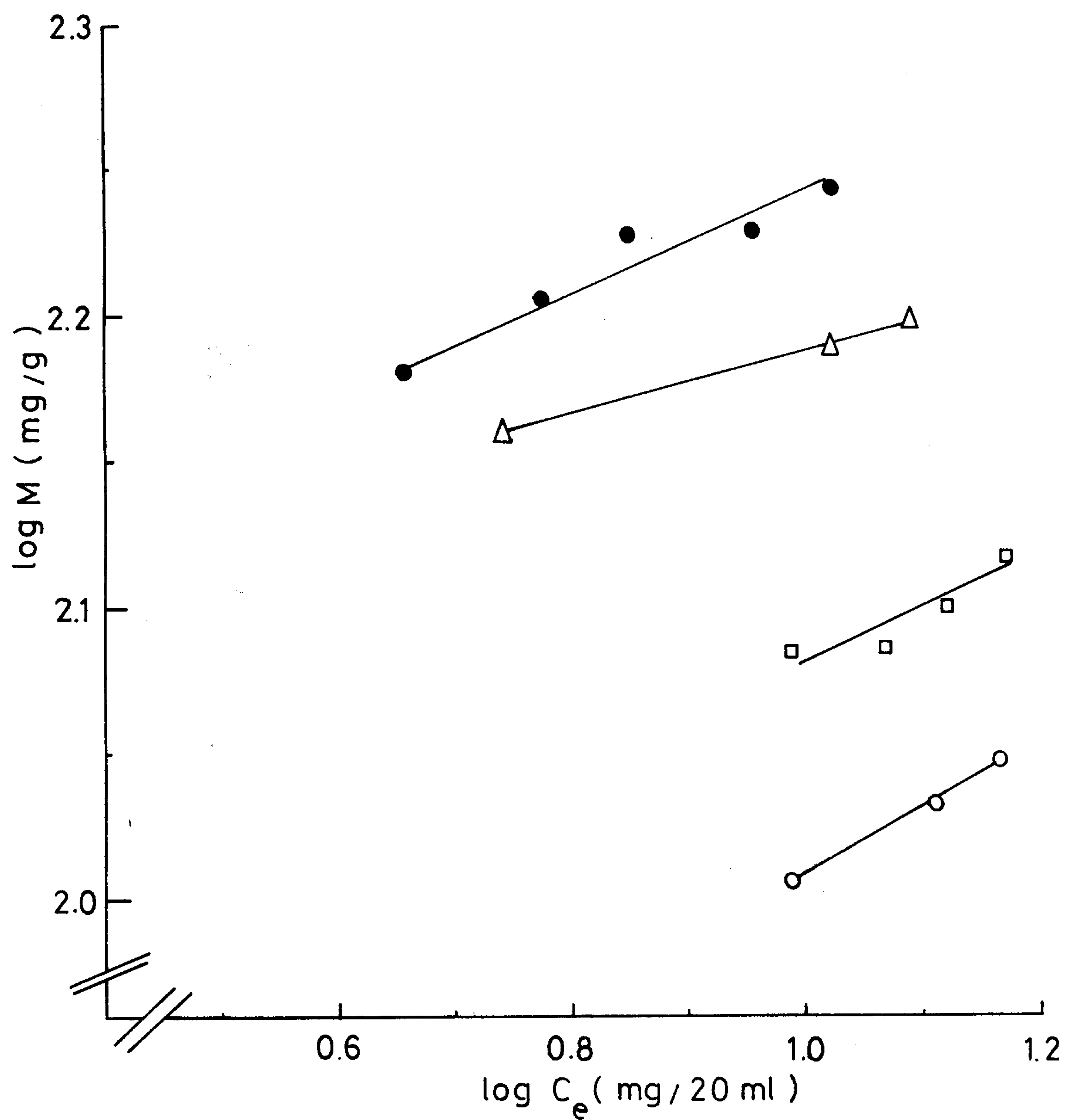


Fig. 6 : Freundlich Adsorption Isotherm for Rifampicin on Activated Charcoal and in the Presence of Different Concentrations of Polysorbate 80.

Key : The same as Fig. 4.

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دراسة معملية على امتزاز الريفامبيسين من محلول مائي

سيد اسماعيل محمد - سهير الشنواني

قسم الصيدلانيات - كلية الصيدلة - جامعة اسـيوط

تم فى هذا البحث دراسة امتزاز الريفامبيسين - من محلوله المائى - على مواد غير قابلة للذوبان فى الماء . وتمثلت هذه المواد فى الكاولين ، التلك ، ثلاثى سيليكات الماغنسيوم ، اكسيد الماغنسيوم ، والافسيل ١.١ . ولقد اجريت جميع التجارب المعملية عند درجة حرارة ٣٠°م ، قيد ٠.٦ وتم اختيار هذا الرقم الهيدروجينى حيث انه انسب قيمة هيدروجينية يكون عندها محلول الريفامبيسين فى حالة ثبات .

اثبتت النتائج ان كمية الريفامبيسين الممتزة تعتمد على طبيعة المادة المستخدمة فى عملية الامتزاز . ولقد وجد ان هذه النتائج مطابقة لكل من معادلتى لانجمايروفريندليش . ويمكن ترتيب هذه المواد حسب قابلية الريفامبيسين للامتزاز على سطحها كالاتى : كاولين > تلك > ثلاثى سيليكات الماغنسيوم > افسيل ١.١ > اكسيد الماغنسيوم .

وتم فى هذا البحث ايضا دراسة تأثير تركيزات مختلفة من عديد سوروبات ٨٠ على درجة امتزاز الريفامبيسين على سطح الفحم النشط ولقد اتضح انه كلما زادت درجة تركيز البولى سوروبات ٨٠ كلما قلت درجة امتزاز الريفامبيسين .

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